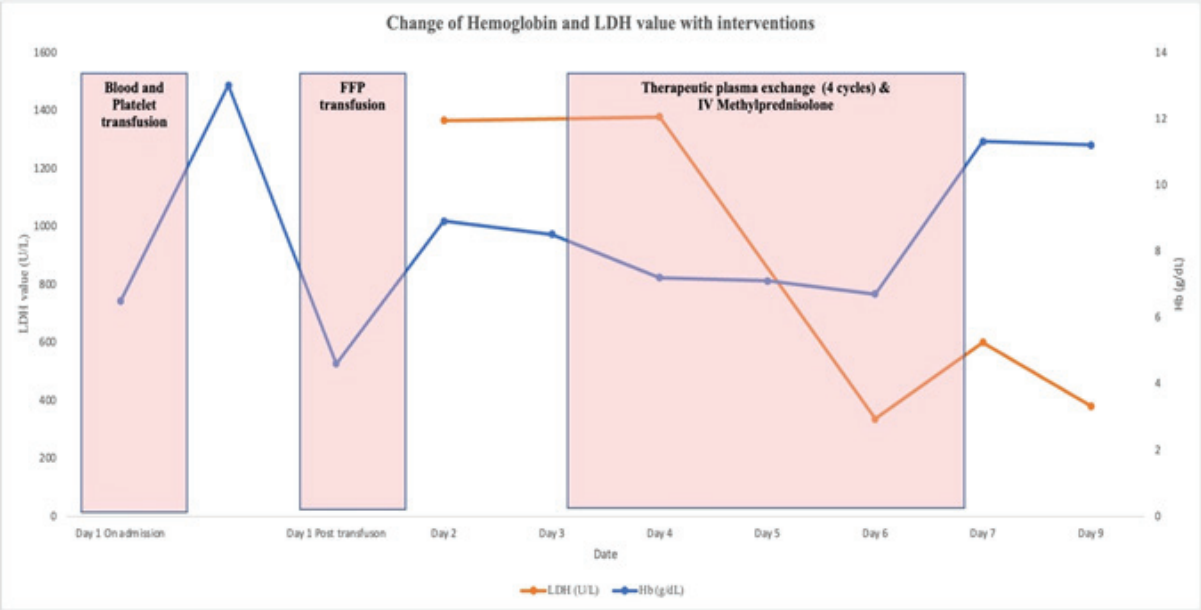
CASE REPORT

Severe Toxin Mediated Thrombotic Microangiopathy after Consumption of Processed Ceylon Olive *(Elaeocarpus serratus)*; A Case Report

Rathnayake K.T.D.P, Jayasinghe J.M.M, Kularathna M.D.S.V and Kularatne S.A.M



Highlights

- A 23-year-old girl presented with severe anemia associated with a history of consuming processed Ceylon olive 4 days back
- Her hemoglobin was 6.5 g/dL and her platelet were $5x10^3/\mu L$ and blood picture showed microangiopathic hemolytic anemia
- She recovered following four cycles of therapeutic plasma exchanges and intravenous methylprednisolone pulses
- Commercial preparation of Ceylon olive may alter its properties, potentially producing toxic compounds linked to immune-mediated thrombotic microangiopathy, highlighting the need for quality control in street-vended foods.

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CASE REPORT

Severe Toxin Mediated Thrombotic Microangiopathy after Consumption of Processed Ceylon Olive *(Elaeocarpus serratus)*; A Case Report

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Abstract: Thrombotic microangiopathy (TMA) is a diverse group of disorders where the pathophysiology is thrombosis in microvasculature. Snake and bee venom-induced TMA is known, but food toxin-induced TMA was not reported. A 23-year-old girl presented with severe anemia after eating processed Ceylon olive (*Elaeocarpus serratus*) 4 days back. Her exposure to any other known causative factor for TMA was excluded. Her hemoglobin was 6.5 g/dL, and her platelet was $5x10^3/\mu L$. She was treated with blood and platelet transfusions. But post-transfusion hemoglobin dropped to 4.5 g/dL, while the platelet count increased to 165 $x10^3/L$, which suggested ongoing hemolysis. The blood picture showed microangiopathic hemolytic anemia. Lactate dehydrogenase (LDH) was very high. She developed acute kidney and lung injuries during the course of her illness and management. With supportive care, four cycles of therapeutic plasma exchanges, and intravenous methylprednisolone pulses, she recovered. This case adds a novel dimension to TMA pathophysiology and management. It underscores the need for clinicians to remain vigilant about atypical causes of TMA including food toxin, which has not been widely reported in medical literature. This also highlights the importance of early diagnosis and intervention such as therapeutic plasma exchange to reduce morbidity and mortality.

***Keywords*:** Ceylon olive; Food toxin; Severe hemolytic anemia; Thrombotic microangiopathy; Therapeutic plasma exchange

INTRODUCTION

Thrombotic microangiopathies (TMAs) are a group of disorders marked by fever, thrombocytopenia, organ dysfunction and acute kidney injury. Laboratory findings include microangiopathic hemolytic anemia with fragmented red blood cells, low haptoglobin, high LDH and thrombocytopenia. These manifestations result from microvascular thrombosis, causing end-organ ischemia. TMAs can be caused by inherited or acquired mechanisms, including complement activation and endothelial damage. The two main types of TMA are thrombotic thrombocytopenic purpura (TTP), caused by ADAMTS13 deficiency, and hemolytic uremic syndrome (HUS), often linked to complement dysregulation. Other causes include infections, drugs, pregnancy complications, and toxins like bee venom and snakebites, though food toxins have not been linked to TMA in medical literature (Azarm, 2021; Begue et al., 1991; Gavriilaki et al., 2019; Karakus et al., 2020; Noutsos et al., 2020; Rathnayaka et al., 2019; Reese et al., 2015; Wijewickrama et al., 2020a).

CASE

We report a 23-year-old young girl admitted to the Emergency Treatment Unit of the Teaching Hospital - Peradeniya in the evening complaining of headache and fever for 3 days. She had a severe right sided frontal headache which did not respond to simple analgesics. Headache was associated with photophobia and phonophobia. She had taken a snack of pickled Ceylon olives (*Elaeocarpus serratus*, Veralu in Sinhala and Ulankarai in Tamil) from a street vendor 5 days prior, which was left unattended for 1 day. It was prepared by boiling the mild- ripened fruit and addition of flavors as desired which were vinegar, chili powder, pepper, salt or sugar as preference. She re-boiled it and consumed a quantity of 25-30 fruits by herself. Following consumption, she had vomiting of undigested food particles with epigastric pain. She had been taking omeprazole, famotidine, and domperidone for a gastritis episode. On admission, she denied cough, cold, shortness of breath, abdominal pain, or loose stools. No history of gastrointestinal or vaginal bleeding. But she admits she had noted Coca-cola-colored urine on the same day evening after consumption of Ceylon olive. She did not have arthralgia, rash, or hair loss suggestive of connective tissue disease. She gave a past history of an episodic headache which aggravated with sunlight and certain food, suggestive of migraine. However, she was not started on any prophylaxis medication.

On examination, she was moderately pale, with a lemon tinge of icterus in the sclera. She did not have lymphadenopathy, hepatosplenomegaly, or neck stiffness. There were no focal neurological deficits. She was hemodynamically stable with no evidence of bleeding manifestations such as mucosal bleeding, petechiae or purpura.

Her full blood count revealed her hemoglobin is 6.5 g/dL with a platelet count of $5\times10^3/L$ while her WBC count is $12.75\times10^3/\mu L$. Urine hCG was negative. A bedside ultrasound scan revealed collapsed inferior vena cava with no free fluid in the abdomen. Her NS1 antigen and IgM for dengue were negative. The working diagnoses were autoimmune hemolytic anemia, B12 deficiency with sinusitis or subarachnoid hemorrhage due to low platelets. Non-contrast computed tomography (CT) of the brain excluded intracerebral hemorrhage.

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She was resuscitated by intravenous normal saline. Urgent blood and platelet transfusions were given as the blood picture was not available until the next morning. A CT venogram was planned for the next day. She was transferred to the medical ward- high dependency unit. A multidisciplinary approach was taken with the involvement of a hematologist, transfusion physician and intensivist. Post-transfusion counts showed hemoglobin further dropped to 4.5 g/dL. The platelets count was $165\times10^3/\mu L$. Though she did not have ongoing dark urine or worsening of lemon tinge icterus, hemolysis was evident with high lactate dehydrogenase level and indirect hyperbilirubinemia. She was not symptomatically improving with transfusions. The direct agglutination test was negative. Retic count was 12.6%. Her blood picture revealed microangiopathic hemolytic anemia with normochromic normocytic anemia, red cell fragments, polychromasia and nucleated red blood cells. C3 and C4 complement levels were normal. TTP was suspected on clinical grounds. An urgent bone marrow aspiration was done, which revealed reactive bone marrow.

Her repeat blood counts came as hemoglobin dropped from 13 to 8.9 g/dL, platelet $132\times10^3/\mu L$ and LDH 1364 U/L. Since the patient was complaining of headache and had ongoing hemolysis with dropping hemoglobin, fresh frozen plasma (FFP) transfusion was given. While on her 1st FFP transfusion, the patient complained of shortness of breath and dropped saturation to 88%, but no features of anaphylaxis. The patient was managed as an allergic reaction to FFP. She improved with oxygen via mask and tailed off to nasal prong oxygen gradually. Her Covid-19 rapid antigen was negative. Empirical antibiotics were started to cover possible atypical pneumonia.

With evidence of ongoing hemolysis, therapeutic plasma exchange and IV Methylprednisolone were planned. Patients got dyspneic and desaturated during 1st therapeutic plasma exchange to 64% while on oxygen. She did not have features suggestive of anaphylaxis. Bedside 2D ECHO did not show any right atrial, right ventricle dilatation or any blood clot suggestive of pulmonary embolism. She was managed as a transfusion-related acute lung injury at intensive care unit. She underwent plasma exchange for 40cc/kg body weight every day and her plasma were replaced with FFP. She received an average exchange of 2500 ml of FFP each day. During the ICU stay, she developed features of renal failure but responded to hydration and diuretics. She underwent 4 cycles of TPE and 3 doses of Methylprednisolone pulses. Following 3rd plasmapheresis, symptoms, signs and laboratory abnormalities improved, and the platelet count got normalized. Meanwhile her Hemoglobin and platelet count stabilized on 10.7 g/dL and $223\times10^3/\mu L$ respectively. LDH value dropped to 599 U/l.

She was discharged on day 15 with advises to be aware of symptoms and inform medical officers about her condition if acute hemolysis relapses. In the follow-up over two years, she remains healthy and avoids Ceylon olive.

DISCUSSION

Our patient presented with TMA, characterized by hemolytic anemia, severe thrombocytopenia and end-organ dysfunction after consuming preserved Ceylon olive fruits. The patient delayed seeking hospital care for four days despite severe anemia. Initial tests revealed a negative direct Coomb's test, suggesting non-immune-mediated hemolysis (Joly et al., 2017; Kucukyurt et al., 2020; Scully et al., 2014). Brain imaging excluded intra-cerebral hemorrhage, but due to limited resources, a CT venogram and ADAMTS13 activity assessment were not performed.

TMA has many differentials, including thrombotic thrombocytopenic purpura (TTP), complement-mediated hemolytic uremic syndrome (HUS), disseminated intravascular coagulation, systemic lupus erythematosus (SLE), antiphospholipid syndrome, vasculitis, pregnancy, malignant hypertension, and infections (e.g., Shiga toxin-producing bacteria, HIV, cytomegalovirus). Drug-induced

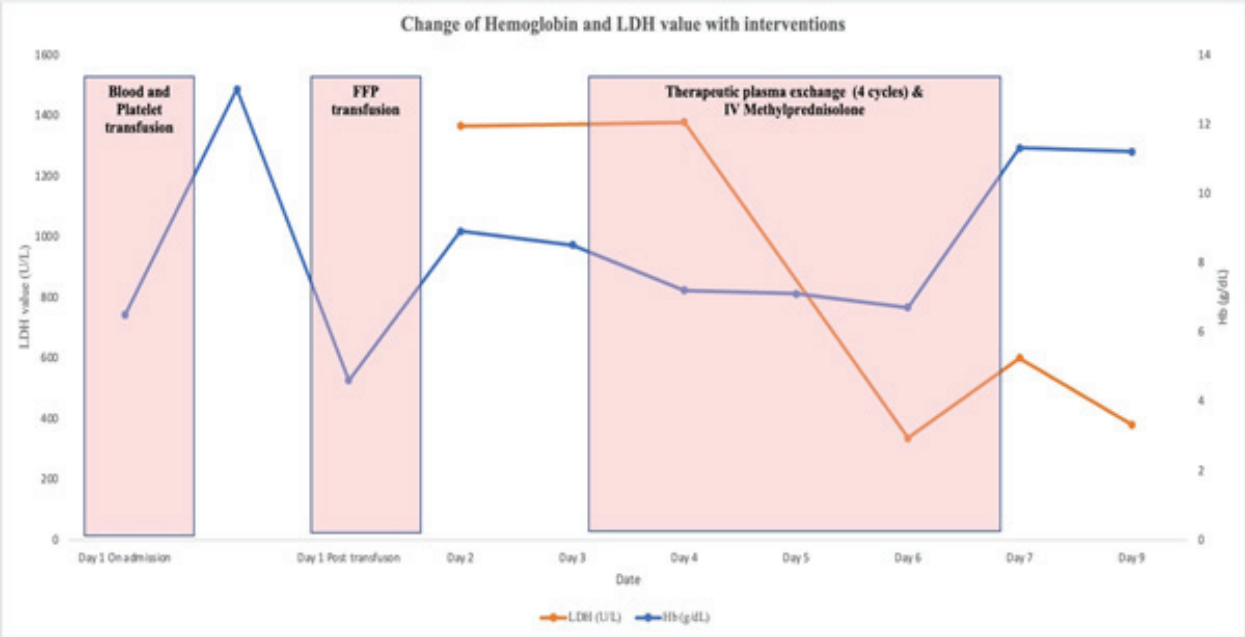


Figure 1: Change of Hemoglobin and LDH values with interventions

TMA can arise from medications such as calcineurin inhibitors, quinine, chemotherapy agents, and others (Azarm, 2021; Evens, 2002; Gavriilaki et al., 2019; Karakus et al., 2020; Reese et al., 2015). Toxins, including venom from certain snakes and bee stings, have also been linked to TMA (Ashley et al., 2003; Begue et al., 1991; Cobcroft et al., 1997; Herath et al., 2012; Valavi et al., 2011; Wijewickrama et al., 2020a; Wijewickrama et al., 2020b; Withana et al., 2014).

TTP is typically caused by an inherited or acquired deficiency of ADAMTS13, an enzyme that cleaves von Willebrand factor (vWF) multimers, preventing excessive platelet aggregation and microthrombi formation. A deficiency of ADAMTS13 leads to platelet aggregation, microthrombi, and subsequent TMA. Complement-mediated TMA, such as atypical HUS, involves unregulated complement activation and endothelial damage. Other causes, like infection-associated and drug-associated TMAs, have different mechanisms, including endothelial damage and immune-mediated reactions.

Ceylon olive *(Elaeocarpus serratus)* is an indigenous fruit tree in Sri Lanka. It is distributed in tropical regions of the Indian, African, and Australian subcontinents. It usually grows in semi-evergreen and evergreen forests. *Elaeocarpus serratus* fruiting occurs around January. It is an edible fruit that is ovoid in shape and 4-5 cm long (*Elaeocarpus serratus*, 2024). It has a pulpy pericarp enclosing a stony seed. Ceylon olives are consumed as ripened fruit, which has a sour- sweet taste or pulp prepared as jam, squash, and jellies or young fruits prepared as pickles (Raji & Siril, 2021). Ceylon olive pulp was assessed by Fernando et al. (2019) and found to have high concentrations of bioactive compounds such as flavonoids, condensed tannins, and carotenoids. Flavonoids, tannins, and phenolic derivative structures allow them to act as free radical scavengers. High carotenoids and vitamin C content also support antioxidant activity. The chromatographic analysis identified beta amyrin kaempferol and quercetin. Beta amyrin is found to have hepatoprotective and anti-inflammatory activity. Kaempferol and quercetin had demonstrated anti-inflammatory activity in acute and chronic inflammatory conditions in vivo (Fernando et al., 2019).

Commercial preparation of pickles involves boiling and addition of vinegar, tamarind, chili powder, peeper, salt or sugar. The street vendor refused use of preservatives or artificial flavors during the process. Microorganisms like lactic acid bacteria, micrococcus, bacilli, yeasts and fungi are crucial for the fermented pickling process and impact the quality of their flavor, texture, color and safety of the final product. The fermentation conditions such as temperature, pH and salt content and screening microbial communities associated should be monitored to ensure product quality (Behara, 2020).

This patient's clinical picture did not precede known etiologies of TMA. Therefore, it was postulated that the patient had an immune-mediated deficiency of von Willebrand factor–cleaving protease activity in plasma or a complement-mediated mechanism triggered by pickled Ceylon olive fruit. It was proven that Ceylon olive contains immune active compounds which may have initiated an acute, immune-mediated reaction, presenting with the sudden onset of severe systemic symptoms. This can also result from dose-dependent reactions which may be acute, caused by a toxic dose of a toxin, or chronic occurring after a few days of administration.

Upon hospital admission, the patient was resuscitated with blood, platelets, and fresh frozen plasma (FFP). Given the possibility of TTP, plasma exchange (TPE) was considered as a treatment, as it helps remove autoantibodies against ADAMTS13 and provides a source of functional ADAMTS13. (Shwartz et al., 2016) TPE is the mainstay of TTP treatment, improving survival from 90% mortality



Figure 2: Ceylon Olive (*Elaeocarpus serratus*) raw fruits (a) pickled Ceylon Olives (b) The street-vended commercial product.

without treatment to 10% with it (Bentley, 2015; Rock et al., 1991; Winters, 2017). In this case, the patient responded well to TPE, and her symptoms of hemolysis disappeared after the third cycle. Methylprednisolone was also administered to suppress autoantibody production (Matsumoto et al., 2017).

However, TPE is associated with risks (Rizvi et al., 2000), including complications like transfusion-related acute lung injury (TRALI), which occurred in this patient after a second exposure to FFP. TRALI is a rare but serious transfusion reaction that can lead to respiratory distress and pulmonary edema. It is caused by neutrophil sequestration and activation in the pulmonary capillaries, leading to damage and leaks in the capillary endothelium. The mortality rate is 5-25% (Kumar, 2016; P'ng, 2008). The patient's TRALI was managed with intensive care, and the remainder of the plasma exchange was completed in the ICU. Other rare but serious complications of this procedure involve complications of central venous access, infections and reactions to FFP (Rizvi et al., 2000).

Another treatment option, rituximab, a monoclonal antibody targeting CD20, has been used as primary treatment of choice or for relapsed or refractory TTP (Matsumoto et al., 2017), but the patient did not require this treatment as she responded to steroids and TPE.

Following the acute phase of treatment, the patient's symptoms resolved, and she was discharged. However, recurrence of TTP is common, with up to 36% of patients experiencing relapses (Bentley, 2015). Relapsing TTP is often associated with a persistent lack of ADAMTS13. Since this case was secondary to food toxin, the patient was advised to avoid consuming Ceylon olive and any other potential triggers. Over the two-year follow-up, the patient remained healthy and had no recurrence of symptoms.

This case introduces a new perspective on TMA pathophysiology and management, emphasizing the need for clinicians to stay alert to atypical causes, such as food toxins, which have been rarely reported in medical literature. It also highlights the critical importance of early diagnosis and interventions like therapeutic plasma exchange to minimize morbidity and mortality.

LIMITATIONS

As mentioned above, we could not measure the ADAMTS 13 levels in this patient as the assay was unavailable in Sri Lanka

DECLARATION OF CONFLICT OF INTEREST

No conflicts of interest, either commercial or professional

AUTHOR CONTRIBUTIONS

Concept and design, data acquisition, drafting and critical revision of this manuscript: **K.T.D.P**.; clinical management of the case, data analysis and critical revision of the intellectual content of the manuscript: **J.M.M., M.D.S.V.**; leading clinician of the medical team and the critical reviewer of the manuscript: **S.A.M.**

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